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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,225	08/02/2001	Glen A. Evans	P-EA 4672	8914
23601	7590	03/11/2004	EXAMINER	
CAMPBELL & FLORES LLP 4370 LA JOLLA VILLAGE DRIVE 7TH FLOOR SAN DIEGO, CA 92122			SLOBODYANSKY, ELIZABETH	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 03/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/922,225	Applicant(s) EVANS, GLEN A.	
	Examiner Elizabeth Slobodyansky, PhD	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 3-30 and 33-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 31 and 32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 August 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>12/26/01; 7/21/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-35 are pending.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1, 2, 31 and 32 in Paper filed December 8, 2003 is acknowledged. The traversal is on the ground(s) that "it is insufficient for an Examiner to assert that patentably distinct inventions are present in order to restrict an application. There are also must be a serious burden on the Examiner to search and examine the entire application. For the reasons set for the below, Applicants respectfully submits that the burden of searching and examining the method claims of Groups I and X together has not been sufficiently established for the restriction to be proper. ... Applicants submits that, while the claims of Group X are patentably distinct from the claims of Group I, a thorough search of the selected claims of Group I, directed to a polypeptide of SEQ ID NO:2 and a method of identifying a compound that modulates the activity a mannosyl transferase, likely will result in art relevant to examination of the claims of Group X, directed to a method of diagnosing or predicting a bipolar disorder using an agent that binds to a mannosyl transferase of SEQ ID NO:2" (Remarks, page 3, emphasis added). This is not found persuasive because methods of Group I and Group X are methods of use of different products, a mannosyl transferase and an agent of an unknown structure. The search and examination of these two Groups together would require additional search of at least classes/subclasses such as 435/6, 7.71 that are not required for examination of Group I

as well as additional search patent and non-patent databases and divergent considerations.

The requirement is still deemed proper and is therefore made FINAL.

Claims 3-30 and 33-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups II-XII, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper filed December 8, 2003.

Claims 1,2, 31 and 32 are under consideration.

Specification

The specification fails to comply 37 CFR 1.821-1-825 that require for each sequence present in the specification to be assigned a sequence identifier. In the instant case, the requirements are not met because, for example, the sequences shown in Figures 2-6 are not assigned the sequence identifiers either in the drawing or in the Brief Description of the Drawings.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

the claimed invention lacks patentable utility.

Claims 1, 2, 31 and 32 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The applicant has asserted utility for the polypeptide of SEQ ID NO:2 (611 amino acids) encoded by the polynucleotide of SEQ ID NO:1 (1961 bp) as a human mannosyl transferase. However, the asserted utility is not specific and substantial. The term mannosyl transferase encompasses structurally different proteins with different mannosyl transferase activities, i.e. substrate specificities. The specification fails to assert what compounds the protein of SEQ ID NO:2 transfers mannosyl to. Mannosyl transferases comprise a highly diverse group of proteins which transfer mannosyl to a wide variety of different compounds including, proteins, carbohydrates and lipids. The sequence search performed at the US PTO did not reveal a substantial homology of SEQ ID NO:2 to any mannosyl transferase protein for which the enzymatic activity has been shown. As such a skilled artisan would not find an assertion that the protein of SEQ ID NO:2 is a mannosyl transferase reasonable without further supporting evidence. No such evidence is presented in the specification. As mannosyl transferases are a large diverse family of enzymes, a mere disclosure that a protein is a mannosyl transferase without a more specific recitation of what type of mannosyl transferase (i.e., what compound(s) are substrates) is insufficient to provide a substantial utility as the skilled artisan would require further research to identify or reasonably confirm a real world context of use. The specification discloses that a disrupted variant of SEQ ID NO:1 may play a role in bipolar disorder, there is no specific and substantial utility for SEQ ID NO:2 as mannosyl transferase. Thus the asserted utility of the claimed polypeptides and its variants is not substantial or specific. For all

the reasons detailed above, the claimed polypeptide of SEQ ID NO:2 lacks a specific, substantial and credible utility.

If the utility for a polypeptide of SEQ ID NO:2 as a mannosyl transferase will be established, the following rejections would still apply.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 31 and 32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a mannosyl transferase of SEQ ID NO:2 or a substantially the same sequence and methods of use thereof. Mannosyl transferases comprise a highly diverse group of proteins which transfer mannosyl to a wide variety of different compounds including, proteins, carbohydrates and lipids. The sequence search performed at the US PTO did not reveal a substantial homology of SEQ ID NO:2 to any mannosyl transferase protein for which the enzymatic activity has been shown. The specification does not teach the specific mannosyl transferase activity of SEQ ID NO:2.

furthermore, due to the recitation of “substantially the same”, claims 1 and 2 are not limited to any amino acid structure. Claim 3 recites the protein comprising SEQ ID NOs: 4, 6 or 8 or a fragment or a variant. Therefore, the genus of claimed mannosyl transferases is described by neither structure nor specific function. Said genus encompasses any polypeptides having any mannosyl transferase activity from any source, both naturally occurring and man made. Furthermore, human proteins are known to have allelic and slicing variants. While the specification teaches a polypeptide of SEQ ID NO:2, it fails to disclose the correlation between structure and function common to all members of the claimed genus of mannosyl transferases. The specification teaches the deletion fragment of aggrecanase-2 protein lacking C-terminal TSP domain having the amino acid sequence of SEQ ID NO:4 (753 residues) and its fragments of SEQ ID NO:6 (752 residues) and SEQ ID NO: 8 (628 residues). Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of having a mannosyl transferase activity.

Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1, 2, 31 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mannosyl transferase of SEQ ID

NO:2 (if its function is established), does not reasonably provide enablement for a mannosyl transferase having an undefined homology to SEQ ID NO: 2 and no specific mannosyl transferase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification does not support the broad scope of the claims which encompass mannosyl transferases of an undefined structures and having any mannosyl transferase activity because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting a specific mannosyl transferase activity; (B) the general tolerance of mannosyl transferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any mannosyl transferase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

The specification teaches a mannosyl transferase having the amino acid sequence of SEQ ID NO:2. Despite knowledge in the art to produce mutations in proteins, the specification fails to provide guidance as to where, and what type of (i.e., what amino acid to substitute into, add to or delete from the known sequence), changes in amino acid residues will result in a desired enzymatic activity. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in a certain activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited.

Furthermore, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen large numbers of mutated proteins or genes where the expectation of obtaining similar activity is unpredictable based on the instant disclosure.

Therefore, one of ordinary skill in the art would require guidance, beyond that provided in the specification, in order to make a mannosyl transferase of any structure and substrate specificity in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 31 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "substantially the same amino acid sequence". The specification defines this term by non-limiting examples (pages 12-13) rendering its metes and bounds unascertainable. Also the term "functional" is unclear as defined by non-limiting examples (pages 13-14).

Further, claim 2 is confusing as reciting a mannosyl transferase further comprising a substrate binding domain. In order for a mannosyl transferase to exhibit its catalytic function implies by the term, it has to bind its substrate first. Thus, its unclear in which way claim 2 limits claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, 31 and 32 are rejected under 35 U.S.C. 102(a) as being anticipated by Wiemann.

Wiemann (GenBank AX086428, March 12, 2001, form PTO-1449 filed July 21, 2003) teach a polynucleotide of 1986 bp nucleotides 14-1974 of which are 100% identical to SEQID NO;1 of the instant invention and which encodes a protein (611

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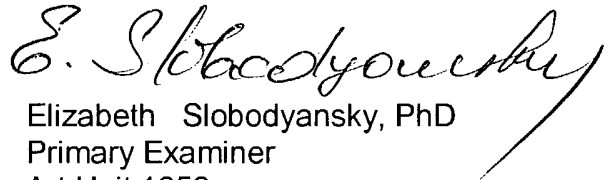
amino acids) of an unknown function having the amino acid 100% identical to SEQ ID

NO:2.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

March 5, 2004